

**DECLARATION**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

5 In re application of: Takahiro ITO et al.  
Serial No. 10/509,912: Group Art Unit: 1623  
Filed: October 4, 2004: Examiner: Jonathan S. Lau  
For: LIQUID PREPARATION COMPRISING CAMPTOTHECIN DERIVATIVE AND  
10 PHARMACEUTICAL COMPOSITION PRODUCIBLE BY LYOPHILIZING THE  
PREPARATION

Honorable Commissioner for Patents

Sir:

15 [A] I, Yasuhiro SHINDO, a citizen of Japan residing 106-1405, Itomachi,  
Chuo-ku, Kobe-shi, Hyogo-ken, Japan, declare as follows:

I graduated from the faculty of agriculture of Kobe University in March,  
1983, and completed the post-graduate/master course of agricultural chemistry  
of Kobe University in March 1985.

20 Since April, 1985, I have been an employee of Mitsubishi Tanabe Pharma  
Corporation (Former Tanabe Seiyaku Co. Ltd.), 2-10 Dosho-machi 3-chome,  
Chuo-ku, Osaka, Japan and I am presently in charge of manager of Patent  
Group 1, Intellectual Property Department of the company.

I am familiar with the subject matter of the invention in this U.S. Serial  
No. 10/509,912.

25 [B] I have studied the paper from the literature cited below and the  
summarized data of T-0128-containing solutions disclosed therein as presented  
in the form of an Attachment (two pages):

"HARADA, Mitsunori et al. Title: Determinants for drug release from T-0128,  
camptothecin analogue-carboxymethyl dextran conjugate, Journal of Controlled  
30 Release 69 (2000) 399-412."

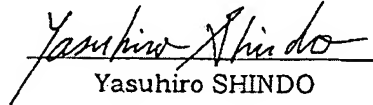
I hereby submit this Declaration into evidence in the present application.

35 [C] I hereby declare that all statements made herein of my own knowledge  
are true and that all statements made on information and belief are believed to  
be true; and further that these statements were made with the knowledge that  
willful false statements and the like so made are punishable by fine or

imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

5

This 8th day of August, 2008

  
Yasuhiro SHINDO

(Attachment)

Appendix: T-0128-containing solution disclosed in Harada et al.

1. Solutions for In vitro Drug Release Tests (Paragraph 2.4 of Harada et al.)

1.1. Solution for hydrolysis stability of T-0128 peptidyl linker to the liver lysosome or homogenate

T-0128 content	100 $\square$ g/mL (5 $\square$ g/mL of T-2513)
pH	4
w/v % of T-0128	0.01
Buffer (mM)	acetate (40)
CaCl <sub>2</sub>	Nil
EDTA	1 mM
Reduced Glutathione	5 mM
Triton X-100	0.1 w/w %

1.2. Solutions for hydrolysis stability of T-0128 to various types of pure enzymes (See Table 1 of Harada et al.)

1.2.1. Solutions for Serine proteinases and Metalloproteinases

T-0128 content: 100 $\square$ g/mL (5 $\square$ g/mL of T-2513)						
pH	3	4	5	6	7	
w/v % of T-0128	0.01	0.01	0.01	0.01	0.01	
Buffer (mM)	acetate (40)	acetate (40)	acetate (40)	phosphate (40)	phosphate (40)	
CaCl <sub>2</sub>	10 mM	10 mM	10 mM	10 mM	10 mM	
EDTA						
Reduced Glutathion						

### 1.2.2. Solutions for Cystine proteases

T-0128 content: 100 $\mu$ g.mL (5 $\mu$ g.mL of T-2513)						
pH	3	4	5	6	7	
w/v % of T-0128	0.01	0.01	0.01	0.01	0.01	
Buffer (mM)	acetate (40)	acetate (40)	acetate (40)	phosphate (40)	phosphate (40)	
CaCl <sub>2</sub>						
EDTA	1 mM	1 mM	1 mM	1 mM	1 mM	1 mM
Reduced Glutathione	5 mM	5 mM	5 mM	5 mM	5 mM	5 mM

### 1.2.3. Solutions for Aspartic proteinases

T-0128 content: 100 g/mL (5 g/mL of T-2513)						
pH	3	4	5	6	7	
w/v % of T-0128	0.01	0.01	0.01	0.01	0.01	
Buffer (mM)	acetate (40)	acetate (40)	acetate (40)	phosphate (40)	phosphate (40)	
CaCl <sub>2</sub>						
EDTA						
Reduced Glutathione						

## 2. Solutions for In vivo inhibition studies (Paragraph 2.5 of Harada et al.)

T-0128 content: 10 mg/mL (0.5 mg/mL of T-2513)	
pH	Not disclosed
w/v % of T-0128 Buffer	1.0 Nill (Solvent: saline)